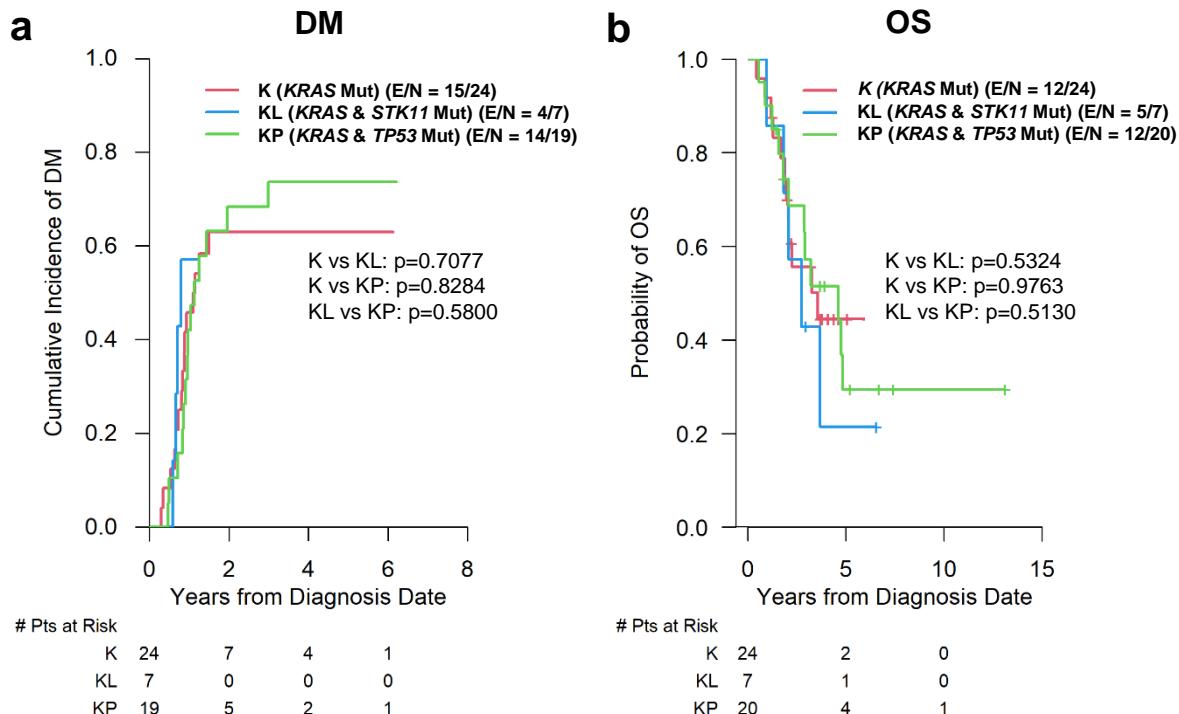
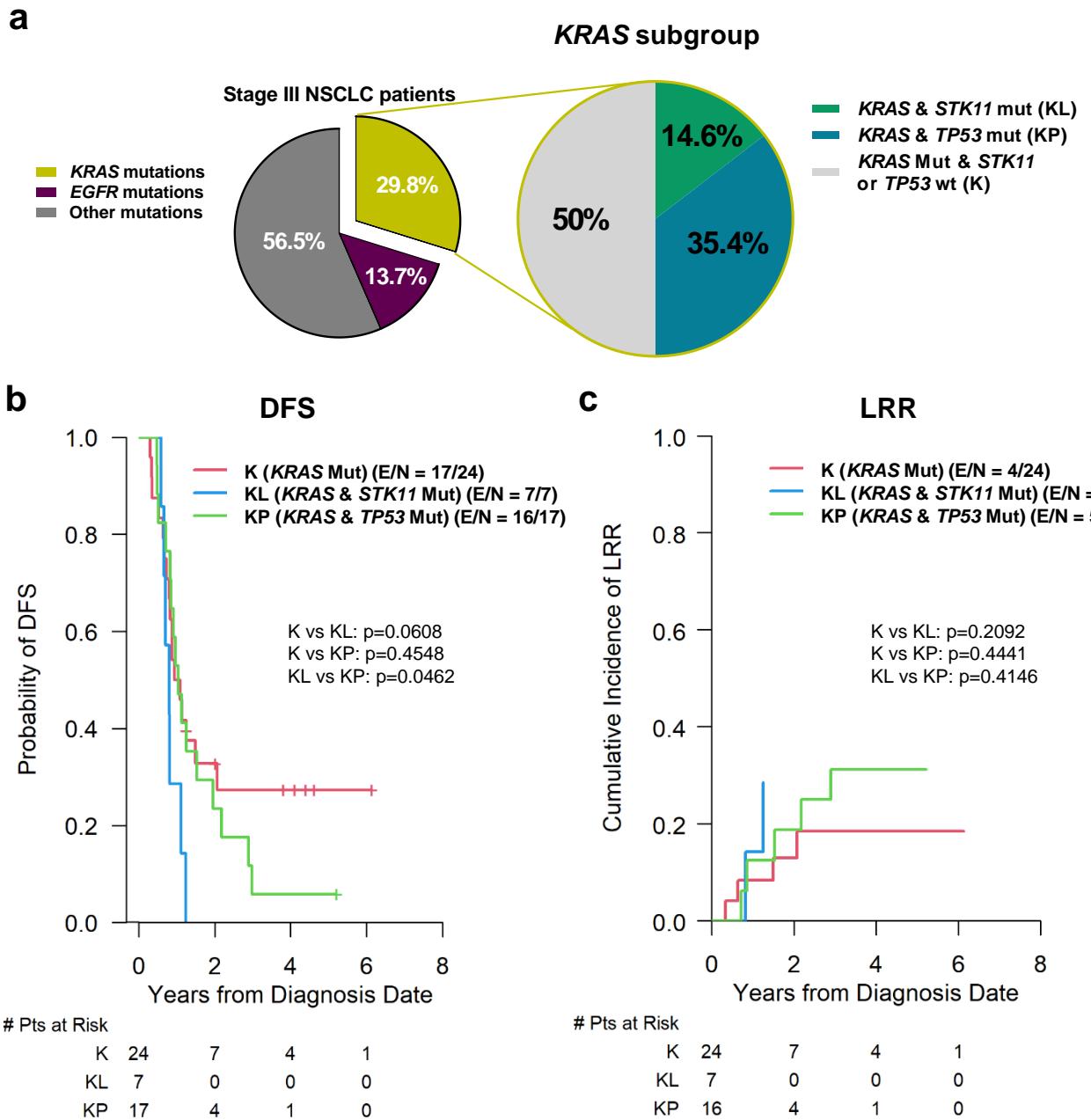


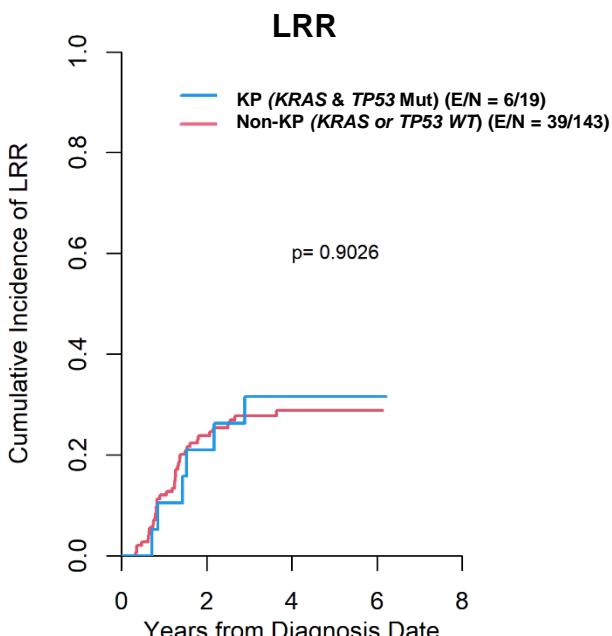
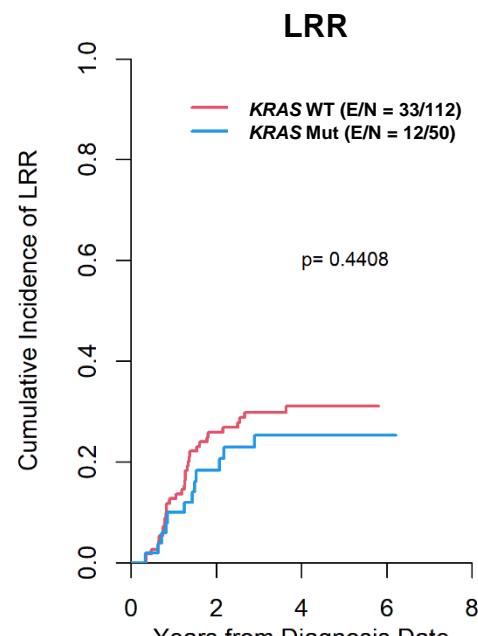
**Supplementary Figure S1. *STK11/LKB1* mutation status predicts chemoradiation outcome in patients with stage III NSCLC.** Estimated cumulative incidence of loco-regional recurrence (LRR) according to *STK11* mutational status in stage III patients with performance status of 0-1 treated with concurrent chemoradiation.



**Supplementary Figure S2. Radiation outcome in *KRAS* mutant patients with stage III NSCLC.** (A) Estimated cumulative incidence curves illustrating distant metastasis (DM) rate and (B) overall survival (OS) by Kaplan-Meier analysis according to *KRAS* mutation subgroup in patients with NSCLC treated with radiation.



**Supplementary Figure S3. Radiation outcome in KRAS mutant patients with non-squamous stage III NSCLC.** (A) KRAS mutation subgroups excluding squamous histology. (B) Disease-free survival (DFS) across KRAS subgroups, and (C) estimated cumulative incidence curves illustrating loco-regional recurrence (LRR) over time according to KRAS mutation subgroup in patients with non-squamous NSCLC treated with radiation.

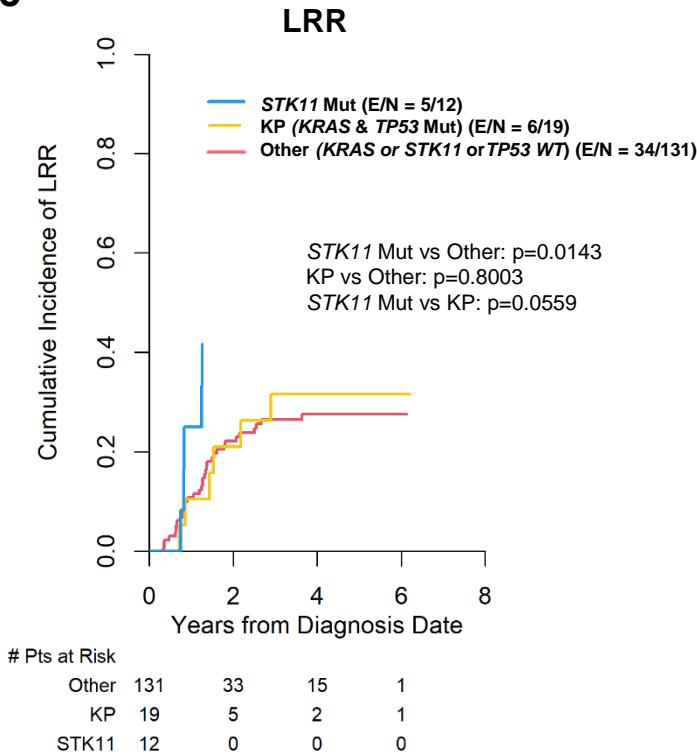
**a****b**

# Pts at Risk

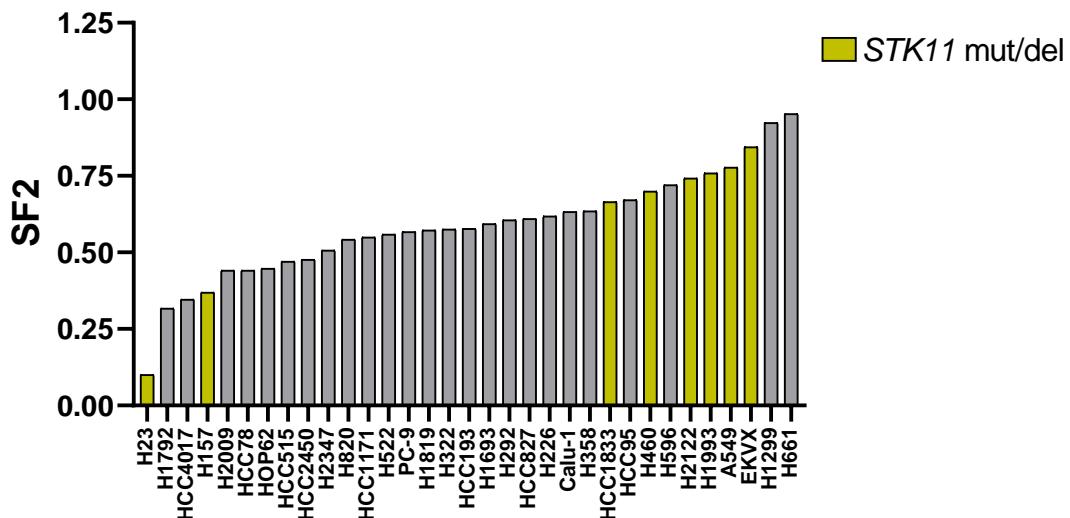
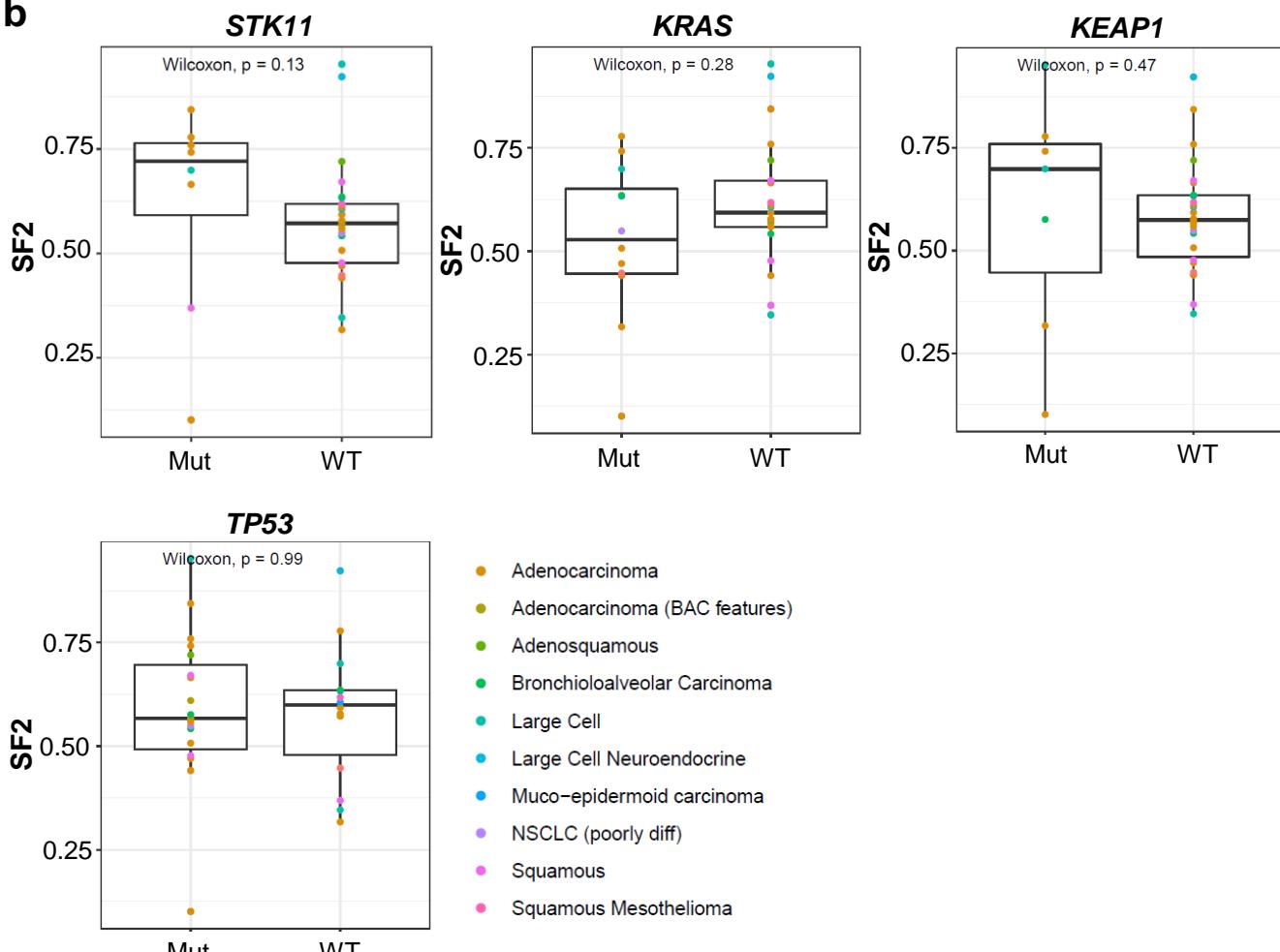
Wild-type	143	33	15	1
Mutant	19	5	2	1

# Pts at Risk

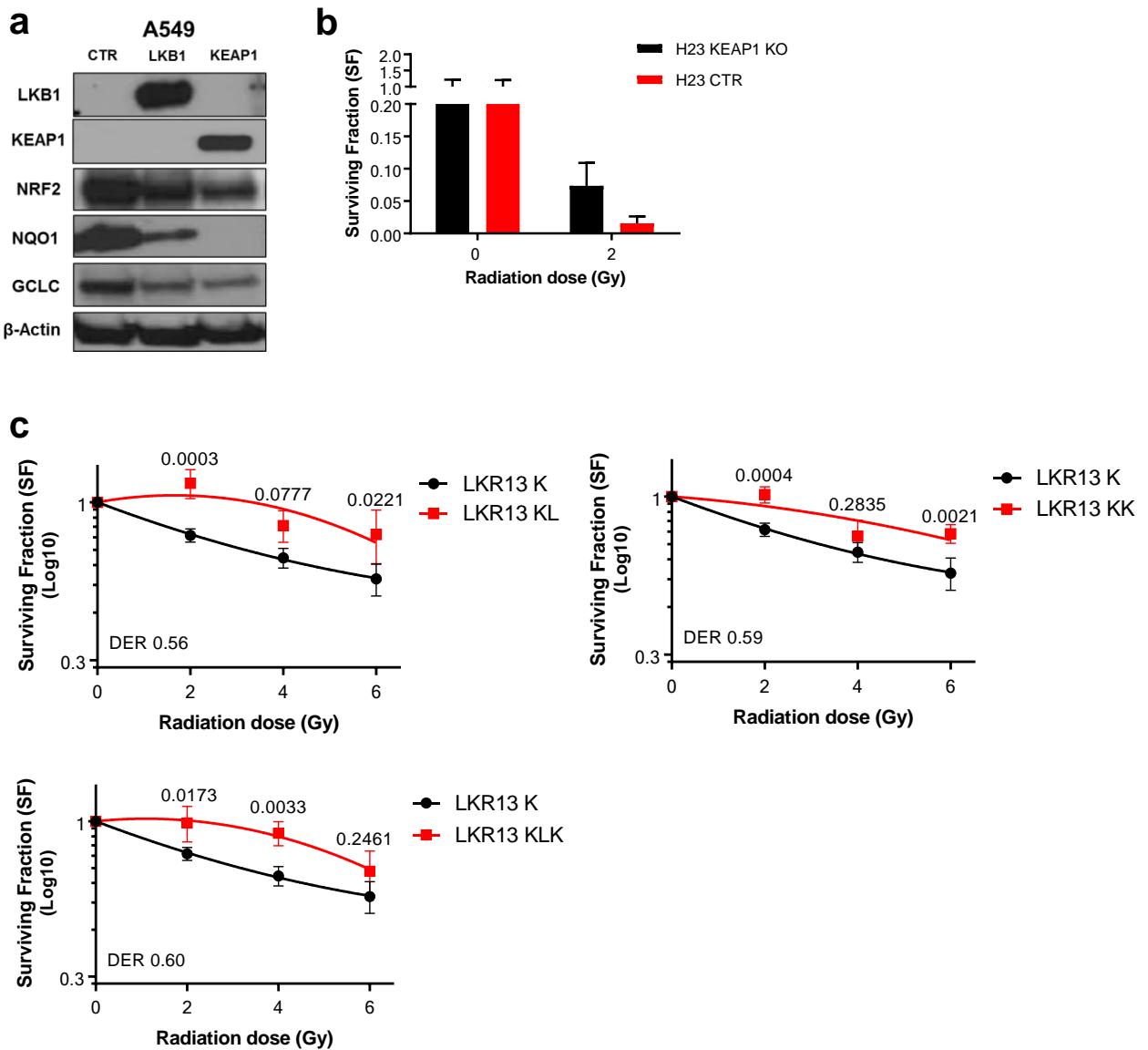
Wild-type	112	26	11	0
Mutant	50	12	6	2

**c**

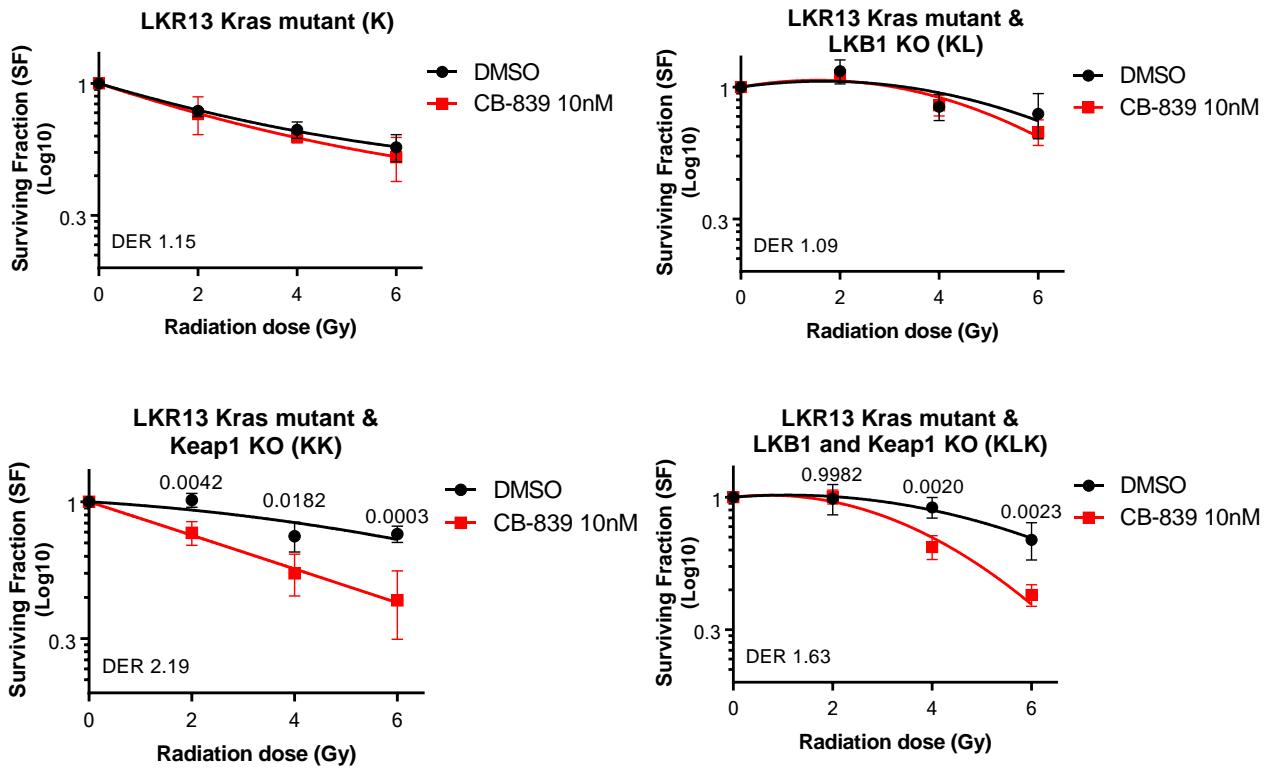
**Supplementary Figure S4. Radiation outcome in patients with stage III NSCLC.**  
Estimated cumulative incidence curves illustrating loco-regional recurrence (LRR) for (A) KP mutant vs non-KP, (B) KRAS mutant vs wild-type, and (C) for indicated mutation status in patients with NSCLC treated with radiation.

**a****b**

**Supplementary Figure S5. *STK11/LKB1* mutation is associated with radiotherapy resistance.** (A) Radiation sensitivities, expressed in terms of surviving fraction at 2 Gy (SF2), of the 33 NSCLC cell lines that formed colonies in culture. (B) Wilcoxon correlation of radiation sensitivities (SF2) and mutations status for indicated genes performed in the 33 NSCLC cell lines. Graphs show median  $\pm$  1.5 interquartile range.



**Supplementary Figure S6.** (A) Expression of LKB1, KEAP1, NRF2, NQO1 and GCLC after stable expression of wild-type LKB1 in LKB1-deficient A549 cell line and wild-type KEAP1 cDNA in the naturally KEAP1-deficient A549 cell line.  $\beta$ -actin was used as loading control. (B) Clonogenic survival assay of stable KEAP1 knockdown in wild-type KEAP1 H23 cell line treated with ionizing irradiation (2 Gy). A representative experiment from 3 or more independent experiments are shown. (C) Quantification of surviving fraction from clonogenic survival assay for LKR13 *Kras* mutant (K); plus LKB1 KO (KL) or KEAP1 KO (KK); or double KO (KLK). Surviving fraction is calculated as the plating efficiency of treated cells divided by plating efficiency of untreated cells. Graphs show 3 biological replicates from one experiment. All data are presented as mean  $\pm$  SEM or SD (panel C); Error bars indicate  $\pm$  SEM or SD (panel C).



**Supplementary Figure S7.** Quantification of surviving fraction from clonogenic survival assay for LKB1 and KEAP1 LKR13 isogenic pairs treated with 10nM of CB-839 for 4 hours. Surviving fraction is calculated as the plating efficiency of treated cells divided by plating efficiency of untreated cells. All data are presented as mean  $\pm$  SD; Error bars indicate  $\pm$  SD. Graphs show 3 biological replicates from one experiment.